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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,489	10/16/2003	Jeffrey M. Linnen	GP140-04.UT	3927

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/688,489	LINNEN ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5- see action*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, and to species wherein the first primer comprises SEQ ID NO: 75, and the second primer comprises SEQ ID NO: 64, in the reply filed on March 15, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Currently, claims 18-30 are pending and under consideration. The claims read on primers for the amplification of nucleic acid sequences in the 3' untranslated region of West Nile virus.

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on January 20, August 19, November 30, and December 20, 2004, and on January 31, 2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

4. The following reference is in a foreign language accompanied by an English abstract. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.

WO 00/66149 (cited in the January 2004 IDS).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 18-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the primer pairs according to claim 26, or primer pairs wherein the first primer comprises 22 contiguous bases with SEQ ID NO: 74 and the second primer is one of those listed (as opposite strand primers) in Table 14 (page 58), does not reasonably provide enablement for amplification kits comprising any primer comprising 22 bases from SEQ ID NO: 74, any primer comprising 18 bases of SEQ ID NO: 59, or any related sequence varying from such sequence by inclusion of a nucleotide analog or up to 10% base variation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The factors considered most relevant in the present case are those of the amount of direction or guidance provided, the presence of working examples, and the nature and predictability of the invention. The present claims read on any combination of two primers for

the amplification of West Nile Virus sequences wherein the first primer comprises at least 22 contiguous bases of SEQ ID NO: 73, including DNA and RNA equivalents, and allowing the presence of nucleotide analogs and up to 10% bases differences; and wherein the second primer comprises at least 18 bases of SEQ ID NO: 59, also including DNA and RNA equivalents, and permitting the same analogs or sequence variation.

The application demonstrates that certain primer fragments from SEQ ID NO: 73 in combination with certain fragments of SEQ ID NO: 59 result in primer pairs capable of amplifying WNV sequences. Page 58. Included in these pairs of primers are embodiments wherein the primer pair includes a primer with a nucleotide analog substituted for a natural base. See e.g., page 32 (disclosing that SEQ ID NO: 65, a fragment of SEQ ID NO: 59, comprises an hypoxanthine for thymine substitution). Thus, the application discloses that certain combinations of the claimed primers are effective for the amplification of WNV nucleic acids.

However, the application also teaches that not every possible primer combination would be so effective. See e.g., pages 58-59 (teaching that the use of other first primer sequences with the opposite strand primers of Table 14 were not effective for the amplification of WNA nucleic acids). Thus, the teachings of the application illustrate that the sequence of the primer used affects the nucleic acid fragment's utility as an amplification primer. The application teaches that not every primer pair is equivalent in their utility for target sequence amplification.

As indicated above, the application demonstrates that certain combinations of the primers were effective for the amplification of WNV target sequences. In each of these cases, the first primer represents all, or a portion of, the first 24 bases of SEQ ID NO: 73. There has been no demonstration that any sequence from the latter 24 bases would be equally effective as a first

primer when used in combination with any fragment of SEQ ID NO: 59. Similarly, SEQ ID NOs: 60, and 62-66, listed in Table 14 as operative second primers when paired to the fragments of SEQ ID NO: 73, do not represent the full scope of possible primer sequences from SEQ ID NO: 59. Nor does the application identify any particular element in the disclosed operative sequences that would enable those in the art to predict which other sequences, or primer pair combinations, would result in effective amplification pairs. Further, the application provides no demonstration that up to 10% of each of these sequences may be substituted for other bases without a loss of such efficacy. Thus, while the application demonstrates enablement for the specific embodiments identified in Table 14, and thereby indicates that the opposite strand primers in the Table would be effective with first primers comprising 22 bases from SEQ ID NO: 74, the application does not demonstrate, and provides no guidance that would lead those in the art to primer pairs other than those in Table 14.

Further, because the application asserts and provides evidence of the unpredictability as to efficacy of different primer sequences, and sequence combinations, the working examples of Table 14 provide little in the way of guidance to other primer pairs. In particular, the application fails to show that any sequence from SEQ ID NOs: 59 and 73, other than those of Table 14, would be effective. Additionally, there is no basis for the assertion that any primer of up to 10% difference from the disclosed primers would retain the same amplification activity.

With reference to the use of sequences comprising nucleotide analogs, while the application shows that the primer of SEQ ID NO: 65, which contains a nucleotide analog, was effective in certain primer pairs (Table 14), there is no demonstration of any other such nucleotide analogs. In particular, SEQ ID NO: 61 is conspicuous in its absence from Table 14,

particularly given the teaching on page 58 that other primer pair combinations not disclosed on Table 14 were found to be inoperative.

In view of the teachings of the application regarding the unpredictability of the art, the limited guidance provided to other operative combinations, and to modifications that may be made to the primers of Table 14 without loss of activity, and because the scope of the operative embodiments are not representative of the full scope of the claimed inventions, the indicated claims are rejected as exceeding the scope of enablement.

7. Claims 18-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a genus of primer pairs, and to analogs or variants thereof, wherein the primer pairs are useful for the amplification of West Nile Virus nucleic acid sequences. The first primer of the primer pair described as any fragment of at least 22 bases from either SEQ ID NO: 73, or SEQ ID NO: 74, and allowing for the presence of nucleotide analogs and up to 10% base variation. The second primer is identified as comprising at least 18 bases from SEQ ID NO: 59, also allowing for allowing for the presence of nucleotide analogs 10% base variation.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. However, it is also noted that the presence of multiple species with in a claimed genus does not necessarily demonstrate possession of the genus in every situation. See, In re Smyth, 178 U.S.P.Q. 279 at 284-85 (CCPA 1973) (stating "where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus or combination claimed at a later date in the prosecution of a patent application."); and University of California v. Eli Lilly and Co., 43 USPQ2d 1398, at 1405 (Fed Cir 1997)(citing Smyth for support).

As was indicated above, the Applicant has provided several working examples (species) of the claim genus. The teachings of the application appear sufficient to provide support for claims drawn to a genus comprising the use of primers according to Table 14, or the use of fragments (comprising 22 bases) of SEQ ID NO: 74 with the opposite strand primers disclosed therein. However, as was also indicated above, these examples illustrate only a portion of the claimed genus. For example, the working examples presented account for only a portion of the

primers from SEQ ID NOs: 59 and 73. Further, because the application demonstrates the operability of only a single claimed primer comprising a nucleotide analog, and indicates that another was inoperative, the application also fails to provide adequate support for primer pairs wherein the primers may comprise any number of nucleotide analogs. The application also fails to provide any demonstration that any primer comprising up to 10% base variation from SEQ ID NOs: 59 or 73 would result in an operable primer.

The limited provision of operable species is particularly important given the teachings in the application which illustrate that there is unpredictability in the performance of other primer pairs than those identified in Table 14. The application's assertion that all primers are not equivalent, that many that were tested resulted were inoperable (pages 58-59), demonstrates uncertainty in the art, and therefore necessitates further description to provide adequate support for the scope of the claimed genus. In the absence of such further support, and for the reasons above, the claims are rejected as lacking adequate written description support for the entirety of the claimed genus.

Conclusion

8. No claims are allowed.

9. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Young et al. U.S. 2004/0229261 (of record in the November 2004 IDS). This reference teaches a primer comprising SEQ ID NO: 75. See e.g., page 3, paragraph [0018], and SEQ ID NO: 2. However, the reference does not teach the pairing of this primer with a sequence from SEQ ID NO: 59. The reference is therefore not applied against the claims.

Kacian et al., U.S. 5,888,779. This reference teaches methods for the amplification of target nucleic acid sequences. The reference teaches the use of target complimentary sequences with a polymerase promoter sequence at its 5' end. See e.g., columns 8-9, and 21. The reference teaches that such amplification may be used in methods for the identification of microorganisms and the diagnosis of diseases. Column 1. However, the reference does not specifically teach the use of such amplification for the detection or identification of West Nile virus.

Ennis et al., U.S. 5,939,254. This reference teaches the use of primers from the 3" non-coding region of Dengue virus (a flavivirus, and therefore related to the West Nile virus) for specific detection of the virus. The reference teaches that the primers from conserved regions of the Dengue virus 3' non-coding region were able to detect the presence of Dengue virus, but did not detect the presence of other flavivirus. See e.g., columns 1, 5-6, 7, and 9. The reference does not indicate whether primers from 3' regions of other flavivirus would be useful in the detection of such other virus. However, Brinton et al. (Virology 153: 113-121) indicates that, although the overall structure of the Flaviviral 3' sequence is preserved, the sequences vary from virus to another. Pages 119-120. From these teachings, those in the art may have been directed to the use of primers from this region for the detection of West Nile Virus. However, the references do not teach or suggest the specific primer pairs presented in the present application. See also, Sherret et al., Emerg Infect Dis 7: 697-705 (teaching that those in the art have classified several viruses as West Nile viruses based, in part, on sequence homology in the NS5/3' untranslated region).

Lanciotti et al., Science, 286:2333-37. This reference discloses West Nile virus genomes by GenBank Accession numbers- at least one of which AF196835, comprises portions of, or complementary sequences to, SEQ ID NO: 59 (bases 10523-10552) and 74 (bases 10606-10629).

NCBI printout of Accession AF196536, a known West Nile sequence disclosed in Sherret et al. (supra.), which comprises SEQ ID NO: 59 (bases 391-421), and the complement to SEQ ID NO: 74 (bases 475-498).

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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